

DR-56. THE DEVELOPMENT OF THE OPTIMAL METHOD OF OBTAINING MAGNETIC LIPOSOMES CARRYING RUBOMYCIN

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One of the significant problems of modern medical and pharmaceuticals chemistry is developing of selective preparations for the targeted delivery of drugs. This problem is most actually for anti-cancer drugs, the high toxicity of which leads to substantial side effects. One of the ways of creating selective anti-cancer drugs is the developing of various types of liposome-encapsulated anti-cancer drugs [1]. The accumulation of liposome drugs in the tumor tissue is caused by the effect of high permeability of the tumor capillaries [2, 3]. The targeted delivery and the selective accumulation of drugs in tumor can be effectively actualized with using magnetic liposome preparations of drugs operated by an external magnetic field. Consequently, developing of magnetic liposomal forms of the known anti-cancer drugs remains a significant interest [4, 5].

The aim of this research is developing of the optimal method to obtain magnetic liposomes carrying daunorubicin on the basis of magnetite (Fe₃O₄) nanoparticles.

By the method of high temperature decomposition of organic iron salt in a high boiling solvent, homogeneous in form and shape magnetite nanoparticles with the average diameter of $7,2 \pm 1,2$ nm were synthesized, capable of forming stable hydrosols without any additional surface modification.

Magnetic liposomes carrying hydrochloride of daunorubicin were obtained by the method of dehydration-rehydration of a thin phospholipid film by hydrosol magnetite with subsequent ultrasonication and freeze-thaw treatment of phospholipid mixtures. The effect of the number of freeze-thaw treatments and the time of ultrasonication on the size and stability of obtained magnetic liposomes was researched and chosen the optimal parameters of a process. The average size of obtained magnetic liposomes carrying daunorubicin equal to $158,2 \pm 31,9$ nm is in the range of 90 to 200 nm, which is optimal for anti-cancer therapy [6].

Synthesized nanoparticles of magnetite and magnetic liposomes loaded with daunorubicin on its basis were characterized by transmission electron microscopy (TEM), selected area electron diffraction (SAED), dynamic light scattering (DLS) and Faraday balance magnetometer.

The obtained magnetic liposomes encapsulated with daunorubicin are perceptively for targeted delivery and accumulation of daunorubicin in tumor.

References

1. Lian T., Ho R. J. Y. Trends and Developments in Liposome Drug Delivery Systems // J. Pharm. Sci. Elsevier, 2001. Vol. 90, № 6. P. 667–680.
2. Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review / H. Maeda [et al.] // J. Control. Release. Elsevier, 2000. Vol. 65, № 1/2. P. 271–284.
3. Malam Y., Loizidou M., Seifalian A. M. Liposomes and nanoparticles: nanosized vehicles for drug delivery in cancer // Trends Pharmacol. Sci. Elsevier, 2009. Vol. 30, № 11. P. 592–599.
4. De Cuyper M., Joniau M. Magnetoliposomes // Eur. Biophys. J. Springer-Verlag, 1988. Vol. 15, № 5. P. 311–319.
5. Thomsen L. B., Thomsen M. S., Moos T. Targeted drug delivery to the brain using magnetic nanoparticles // Ther. Deliv. Future Science Ltd., London, UK, 2015. Vol. 6, № 10. P. 1145–1155.
6. Liposomes in targeting of antitumor preparations / O. I. Sakvina [et al.] // Russian Bioterapevtic J. 2008. Vol. 7, № 4. P. 80–85.